

## **REMARKS**

Claims 34-38 and 40-45 are pending in the application and claims 1-33 and 39 have been canceled. Claims 44-45 have been added. Support for added claims 44-45 can be found in the specification as filed on page 4, second to last paragraph. Applicants respectfully request entry and consideration of the added claims because they require no further search and merely further define the claimed subject matter. Additionally, the new claims place the application in condition for Appeal. Accordingly, entry and consideration of the added claims respectfully is requested.

In the February 15, 2007 Office Action, claims 34-38 and 40-43 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Krebber et al. (1997) *J. Mol. Biol.* 268:607-618 (cited in the IDS) as evidenced by Weiner and Chun (1997) *J. of Comparative Neurology* 381(2):130-142 in view of Mersmann et al. (1998) *J. of Immunological Methods* 220:51-58. The specific grounds for rejection, and applicants' response thereto, are set forth in detail below.

### **Rejections Under 35 U.S.C. §103(a)**

Claims 34-38 and 40-43 are rejected under 35 U.S.C. §103 as obvious over Krebber, as evidenced by Weiner and Chun, in view of Mersmann. Specifically, the Examiner asserts that Krebber teaches nucleic acids encoding a gene III N-terminal protein linked to a 10 amino acid purification tag, but admits that Krebber fails to disclose nucleic acids encoding the gene III fragment linked to a sequence that is 100 to 2000 base pairs long. This deficiency allegedly is remedied by Mersmann, which allegedly discloses nucleic acids encoding gene III linked to antibody chains where the nucleic acid encoding the antibody chain is 100-2000 base pairs long. Applicants respectfully traverse.

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so. *In re Kahn*, 441 F.3d 977, 986, 78 USPQ2d 1329, 1335 (Fed. Cir. 2006) (discussing rationale underlying the motivation-suggestion-teaching requirement as a guard against using hindsight in an obviousness analysis). The teaching, suggestion, or motivation must be found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the

problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). See also *In re Lee*, 277 F.3d 1338, 1342-44, 61 USPQ2d 1430, 1433-34 (Fed. Cir. 2002) (discussing the importance of relying on objective evidence and making specific factual findings with respect to the motivation to combine references); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). MPEP 2143.01 Here, applicants respectfully submit that one skilled in the art would have had no motivation to combine the cited references and, therefore, no *prima facie* obviousness exists and the rejection should be withdrawn.

The instant claims recite a nucleic acid molecule encoding a fusion protein comprising the first N-terminal domain of the gene III protein of filamentous phage and a (poly)peptide which is encoded by a nucleic acid sequence comprised in a genomic DNA fragment or an expressed sequence tag (EST). The gene III fusion partner is derived from a eukaryotic cell and is 100-2000 base pairs in length. The fusion protein lacks a signal sequence for transport of the fusion protein to the bacterial periplasm. Krebber is mainly concerned with gene III fusions that contain a signal sequence, but also describes a nucleic acid encoding an N-terminal domain of gene III attached to a short 10-amino acid histidine tag (see, Figure 3d), that is used for purifying the gene III protein.<sup>1</sup> This particular construct lacks a signal sequence, but nothing in Krebber teaches or suggests using a fusion partner for the gene III protein that is any longer than the short purification tag while simultaneously lacking a signal sequence.

While acknowledging that Krebber fails to teach gene III fusions where the fusion partner has the length recited in the instant claims, the Examiner asserts that Mersmann remedies this deficiency by teaching fusions with antibody fragments having the length recited in the instant claims. However, the Examiner is combining apples and oranges: one of ordinary skill in the art would not have been motivated to combine the nucleic acid disclosed by Krebber, where the construct lacks a signal sequence, with the nucleic acid disclosed by Mersmann, where all the constructs contain a signal sequence. The instant claims explicitly recite that the claimed nucleic acid molecule lacks a signal sequence for transport of the fusion protein to the bacterial periplasm. There is no suggestion in Mersmann to prepare a construct lacking a signal sequence

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<sup>1</sup> Indeed, the Examiner acknowledges that histidine tags are used simply for purification purposes, stating that "[t]he poly (HHHHH) histidine tails are well known tags used in the art. These histidine tags are fused to the protein to facilitate the subsequent purification of the fusion protein in combination with immobilized metal ion affinity chromatography." Office action at page 4.

– indeed, the opposite is true since Mersmann deals with classic display methodology where gene III fusion proteins are transported to the bacterial periplasm to combine with other phage proteins to make phage particles. In this sense, Mersmann can be seen as teaching away from the instantly claimed invention by teaching that gene III fusion proteins should contain a signal sequence.

It is axiomatic that it is improper to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art. In the instant case, the combination of Krebber and Mersmann is improper because it ignores the key distinction that the fusion proteins described by Mersmann all contain a signal sequence. For at least these reasons, there would have been no motivation for one of ordinary skill in the art to combine Mersmann with Krebber and the rejection is improper and should be withdrawn.

**CONCLUSION**

In view of the foregoing amendments and remarks, applicants respectfully submit that the application is in condition for allowance. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact the undersigned to expedite prosecution of the application.

The Commissioner is hereby authorized by this paper to charge any fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-3840. **This paragraph is intended to be a CONSTRUCTIVE PETITION FOR EXTENSION OF TIME in accordance with 37 C.F.R. § 1.136(a)(3).**

Respectfully submitted,



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